IN THE UNITED STATES PATENT AND TRADEMARK OFFICE PATENT

ASSISTANT COMMISSIONER OF PATENTS Docket No. P06477USO/DEJ

Washington, D.C. 20231
S I R:

Transmitted herewith for filing is a **NEW PATENT APPLICATION** under 37 CFR 1.53(b)
Of: HARRIS, Martin Russel
for: COMPACT CONFOCAL ENDOSCOPE AND ENDOMICROSCOPE METHOD AND APPARATUS

Enclosed are the following:

X Specification, abstract and claims of 33 pages
X Drawings: 4 sheets which are declared to be: X formal ___ informal
___ there are no drawings
X Declaration signed by the inventor(s)
X Small Entity Statement
X Assignment Papers
X Certified Copy of Priority Document(s)
___ Preliminary Amendment (reducing the filing fee)
___ Information Disclosure Statement
___ Other:

Note: Address all correspondence to DOUGLAS E. JACKSON at the below address of Customer No. **000881**.

The filing fee is calculated below (after reduction for preliminary amendment if noted above).

		NOW	*Basic Number*	*Present Extra*	*Rate*	$
X	TOTAL CLAIMS	46	- 20	26	X $ 18 =	468
X	INDEP. CLAIMS	5	- 3	2	X $ 78 =	156
	MULTIPLE DEPENDENT CLAIM(S)				+ $ 260 =	
X				BASIC FEE	760 =	760
				TOTAL OF ABOVE CALCULATIONS	=	1384
X	Reduction by ½ for filing of small entity statement				–	692
				SUBTOTAL	=	692
X	Fee for recording of assignment				+ 40	40
				TOTAL OF ALL FEES	=	**732**

X A check in the amount of $ 732.00 is enclosed. If no check or an insufficient check is enclosed and a fee is due in connection herewith, the Commissioner is authorized to charge any fee or additional fee due in connection herewith to Deposit Account No. 12-0555. A duplicate of this sheet is enclosed.

Respectfully submitted,

Date: August 25, 1999

Douglas E. Jackson
By: Douglas E. Jackson
Registration No.: 28518

LARSON & TAYLOR • 1199 North Fairfax St. • Suite 900 • Alexandria, VA 22314

PTO/SB/10 (12-97)
Approved for use through 9/30/00. OMB 0651-0031
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) & 1.27(c))—SMALL BUSINESS CONCERN

Docket Number (Optional) POA77US0/DEJ

Applicant, Patentee, or Identifier: MARTIN RUSSELL HARRIS
Application or Patent No.: NEW Application
Filed or Issued: ON EVEN DATE
Title: COMPACT CONFOCAL ENDOMICROSCOPE AND ENDOMICROSCHOPE METHOD AND APPARATUS

I hereby state that I am
- ☐ the owner of the small business concern identified below:
- ☒ an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN OPTISCAN PTY LTD

ADDRESS OF SMALL BUSINESS CONCERN 27 NORMANBY ROAD, NOTTING HILL VICTORIA 3168, AUSTRALIA

I hereby state that the above identified small business concern qualifies as a small business concern as defined in 13 CFR Part 121 for purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time, or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby state that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

- ☒ the specification filed herewith with title as listed above.
- ☐ the application identified above.
- ☐ the patent identified above.

If the rights held by the above identified small business concern are not exclusive, each individual, concern, or organization having rights in the invention must file separate statements as to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern, or organization having any rights in the invention is listed below:
- ☒ no such person, concern, or organization exists.
- ☐ each such person, concern, or organization is listed below.

Separate statements are required from each named person, concern or organization having rights to the invention stating their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

NAME OF PERSON SIGNING MARTIN RUSSELL HARRIS

TITLE OF PERSON IF OTHER THAN OWNER DIRECTOR

ADDRESS OF PERSON SIGNING 163 PEEL STREET, WINDSON VICTORIA 3181, AUSTRALIA

SIGNATURE Martin Harris DATE 28 - July - 1999

COMPACT CONFOCAL ENDOSCOPE AND ENDOMICROSCOPE METHOD AND APPARATUS

The present invention relates to compact confocal endoscopes and microscopes (including endomicroscopes), of particular but by no means exclusive application in the internal examination of the human body.

Existing confocal endoscopes employ beam splitting apparatus comprising partially mirrored surfaces or compound prisms. Such apparatus are both relatively bulky and designed to function efficiently only when the two exit beams diverge at a relatively high angle (which is often approximately 90°). Conventional beam splitters are generally 45° cubes or pellicles or are near orthogonal to the optic axis (as in the F900e) to eliminate polarisation state noise.

These configurations, however, render a beam splitting head bulky, as suitable photoreceptors or light conduits must be located almost perpendicular to the light source and/or incident light beam. The resulting beam splitter may not, therefore, be deployed in particularly narrow apertures or other sites with restricted access, and nor may it be located on an endoscope head. To do so would increase the space required around the endoscope head, limiting the range of locations in which the endoscope could be deployed. Further, this would increase the mass of such an endoscope head, rendering it unwieldy for some applications. Additionally, beam splitters of this type - with such highly divergent outgoing beams - cannot be readily used where the photo emitter (be it a laser, optical fibre or otherwise) is to be moved in order to scan the sample. Clearly the light receiving means (which may be a pinhole, optical fibre or some form of photo-detector) must be moved in such applications in synchrony with the photo emitter. However, accurately maintaining

such registration where existing beam splitters are employed is impractical, owing to the separation of source and exit beams (and hence or emitter and receiving means).

It is an object of the present invention, therefore, to provide a confocal endoscope beam splitting method and apparatus that at least partially overcomes one or more of the above disadvantages of existing devices.

Accordingly, the present invention provides a confocal endoscope or microscope including:

a light source of coherent light for illuminating a sample;

a beam splitter; and

light receiving means, wherein an incident beam of light from said light source is directed onto said beam splitter and hence onto said sample, and light returning from said sample and incident on said beam splitter is deviated or displaced by said beam splitter by a small angle or distance relative to said incident beam, and received by said light receiving means located to receive said returning light and near said light source.

The beam splitter may be provided by any suitable means, including single or compound prism(s) and/or lens(es). It should be noted that the light returning from the sample may include both fluorescent and reflected light; some beam splitters are envisaged (as will be detailed below) that will provide suitable deviation of the fluorescent light, while others are envisaged that will provide suitable deviation of the reflected light, or of both fluorescent and reflected light. It should also be noted that the light received by the light receiving means will generally be only a portion of the total returning light from the sample. Further, references to an "endoscope or microscope" should be understood to include reference to an endomicroscope.

In one embodiment the light source comprises a mirror located in the path of the returning light for directing light towards the sample, wherein the mirror has a smaller solid angle than the returning light to only partially occlude reception of the returning light by the light receiving means. Thus, in this embodiment the beam splitter is also provided by the mirror, which allows some of the returning to continue to the light receiving means. Preferably the mirror and the light source are provided on a single piece of silicon and the mirror comprises an etched mirror surface of the silicon.

Preferably the endoscope or microscope includes an optical head and said light source is located in or on said head.

Preferably said endoscope or microscope includes heating means for maintaining said head at a temperature substantially equal to that of said sample.

This temperature will, for human samples *in vivo*, human body temperature. This is desirable for patient comfort as well as for the stability of operation of the head components.

Preferably said light source and said light receiving means are on a single mounting means.

Preferably said beam splitter is mounted on said mounting means.

Preferably said mounting means is moveable for scanning said light source.

Thus, in one embodiment the light source, light receiving means and beam splitter are all mounted on the mounting, which is moveable for scanning the light source over the

sample.

Preferably said mounting means includes a reed, and more preferably said mounting means is an electromagnetically vibrated reed.

Preferably said light source and said light receiving means are adjacent or touching.

Preferably said light source is an optical fibre tip.

Alternatively said light source is a laser, and more preferably a blue light laser.

Preferably said beam splitter includes a plurality of prisms and/or lenses.

Preferably said plurality of prisms and/or lenses provide minimal net deviation or translation, so that said coherent light or light reflected from said sample emerges from said plurality of prisms and/or lenses substantially parallel to and optically coaxial with its path immediately before impinging said plurality of prisms and/or lenses.

Thus, the plurality of prisms and/or lenses acts as a "direct vision" spectroscope.

Preferably said plurality of prisms and/or lenses is arranged to focus confocal return stokes fluorescence to form a line, said line forming a spectrum in which shorter wavelength fluorescence is located towards a first end of said line closer to said light source, while longer wavelength fluorescence is located towards a second end further from said light source.

Preferably said endoscope or microscope further includes

means to allow light on either side of a spectral line in said returning light to be included with light from said spectral line when said returning light impinges on said light receiving means.

Preferably said means is controlled by a mechanism which occludes light which is more distant in wavelength than a desired amount from said spectral line, to allow control of depth of field isolation.

Preferably the endoscope or microscope includes optical elements to divert chosen wavelength portions of said spectral line (and optionally light close in wavelength to said spectral line) to one or more photodetectors to give different spectral channels for imaging.

Preferably the endoscope or microscope includes at least one optical waveguide channel to convey said returning light to said photodetectors.

Preferably the endoscope or microscope includes a laser and an optical waveguide to convey light from said laser to said light source.

Preferably the endoscope or microscope includes a first optic waveguide to convey light to said specimen and at least one second optic waveguide channel to convey said returning light to said photodetectors, and said beam splitter is disposed in said head between said first and second optic waveguides.

Alternatively the endoscope or microscope includes a return fibre and said beam splitter is located between a light exit area of said return fibre and said photodetectors, to provide spectral separation after said returning light exits said fibre.

Preferably the endoscope or microscope includes an aperture slit moveable in front of said photodetectors simultaneously with said scanning to compensate for changes in beam splitter deviation.

Preferably said lenses include at least one apochromatic lens.

Preferably said prisms and/or lenses include an SF 11 or SF 59 prism.

Such a combination is reasonably achromatic and non-deviating for the 515 nm - 650 nm range, and which has substantial dispersion for the blue.

According to the present invention there is also provided a method for performing confocal endoscopy or microscopy including:

illuminating a sample by means of an incident or excitatory beam of coherent light; and

deviating or displacing light returning from said sample by a small angle or distance relative to said incident beam.

Preferably said method includes receiving or detecting said returning light at a point close to a source of said incident or excitatory beam.

Preferably said deviating or displacing of said light returning from said sample is effected by means of a beam splitter.

The present invention also provides a confocal endoscope or microscope including:

a light source of coherent light for illuminating a sample;

a beam splitter; and

light receiving means, wherein an incident beam of light from said light source is directed onto said beam splitter and hence onto said sample, and light returning from said sample and incident on said beam splitter is deviated by said beam splitter by a small angle relative to said incident beam, and received by said light receiving means located to receive said returning light and near said light source, and said beam splitter includes polarisation rotating means and deviation means to separate light of different polarisations, and operates by optically rotating said coherent light and said returning light.

Preferably the polarisation rotating means is based on optical rotary dispersion and includes a chiral medium to optically rotate said coherent light and said returning light.

Alternatively the polarisation rotation means includes a Faraday effect material, said material having simultaneously magnetic lines of force in the same direction as the propagation direction of said light, whereby the E vector of said coherent light is rotated as it passes through said material .

Alternatively the polarisation rotation means includes phase plates or retardation elements, of a material whose structure is anisotropic at a molecular or crystalline level.

Alternatively the polarisation rotation means includes liquid crystals.

Preferably said liquid crystals are optically active and/or birefringent.

Preferably said liquid crystals are cholesteric liquid

crystals.

In one preferred embodiment said optical rotation is provided by intrinsic polarisation properties of the sample or of any intermediate optical medium.

Thus, as many biological materials exhibit birefringent properties and or produce optical rotation, it is possible to use this property in the present invention.

The invention also provides a method for maintaining registration in a confocal endoscope or microscope including a light source and a light receiving means, including:

splitting light returned from a sample with a small angle deviation beam splitter;

employing said light source and said light receiving means located on a single moveable mounting means;

moving said mounting means to scan said light source and thereby said sample.

Preferably said beam splitter includes a plurality of prisms and/or lenses.

Preferably the method includes moving said beam splitter with said light source and said light receiving means.

Preferably said plurality of prisms and/or lenses provide minimal net deviation.

Preferably said moving of said mounting means comprises vibrating said mounting means.

Preferably said mounting means is a reed.

Preferably said mounting means is an electromagnetically

vibrated reed.

The present invention also provides a method for performing confocal endoscopy or microscopy including:

illuminating a sample by means of an incident or excitatory beam of coherent light and thereby inducing a broader beam of returning light; and

detecting a portion of the returning light adjacent to or near the incident beam.

Preferably the method includes directing the incident light towards the sample by means of a mirror located in the path of the returning light, wherein the mirror has a smaller solid angle than the returning light to only partially occlude reception of the returning light. Preferably the mirror and the source of the incident light are provided on a single piece of silicon and the mirror comprises an etched mirror surface of the silicon.

In order that the present invention may be more clearly ascertained, preferred embodiments will now be described, by way of example, with reference to the accompanying drawing in which:

Figure 1 is a schematic view of a confocal endoscope according to a preferred embodiment of the present invention;

Figure 2 is a schematic view of the optical configuration of an endoscope head according to another preferred embodiment of the present invention;

Figure 3 is a schematic view of the optical configuration of an endoscope head according to another preferred embodiment of the present invention;

Figure 4 is a schematic view of the optical configuration of an endoscope head according to another preferred embodiment of the present invention;

Figure 5 is a ray trace of the prism combination of figure 4;

Figure 6 is a schematic view of the optical configuration of an endoscope head according to another preferred embodiment of the present invention;

Figure 7 is a schematic view of the optical configuration of the beam splitter of an endoscope head according to another preferred embodiment of the present invention;

Figure 8 is a schematic view of the optical configuration of an endoscope head according to another preferred embodiment of the present invention;

Figure 9 is a schematic view of the Faraday effect optical rotator of an endoscope head according to another preferred embodiment of the present invention.

Figure 10 is schematic view of the head of a confocal endoscope according to a further preferred embodiment of the present invention, in which the light source, optic fibre tip and beam splitter are mounted on the same scanning mechanism; and

Figure 11 is a schematic view of a confocal endoscope according to a further preferred embodiment of the present invention, in which the beam splitter comprises a single piece of silicon with an etched mirror surface.

A confocal endoscope according to a preferred embodiment of the present invention is illustrated schematically at 10 in figure 1. The Endoscope 10 includes a miniature laser diode 12, a scanning mechanism 14, an astigmatism corrector 16, a lens 18 and a Nomarski type polarisation separation prism, often referred to as a Spatial Walkoff Filter (SWF) 20.

A laser beam is generated by the laser diode 12, which is mounted on the scanning mechanism 14. The divergent laser beam passes through the astigmatism corrector 16 to lens 18 which roughly collimates the beam. The collimated beam 34 then passes through the SWF 20.

The polarisation axis of the beam is aligned to the SWF 20 so that there is no separation of orthogonal polarisation vectors of the laser beam, and the beam then passes through a pair of Kerr cells 22 and 24 to lens 26, which focusses the beam to a Gaussian waist 30 within a specimen 28.

Return light, either fluorescence or reflection from the entire interaction volume (a diabolo shaped volume) within the specimen, returns through lens 26. However only light from the Gaussian waist 30 will exclusively retrace the full set of incoming ray paths through the optical system back to the SWF 20.

For imaging in reflection, a current is passed through coil 32 surrounding Kerr cell 22 so that the combined effect on Kerr Cell 22 and Kerr Cell 24 is to rotate the E vector of the polarised return light by 90° degrees relative to the outgoing light. Hence, when the return beam traverses SWF 20 it is diverged from the outgoing beam path 34 and instead it travels along beam path 36.

This returning beam is converged by lens 18 to a focus 38 which causes it to enter the core at the tip of an optic fibre 40.

The return light is carried in the core of fibre 40 to the opposite end 42, from which it is emitted and passes to photomultiplier tube (PMT) 44. The electrical output of PMT 44 in conjunction with the XY positional information from the scanning mechanism 14 is used to build up a 2D data set forming the image.

In fluorescence imaging mode the current in coil 32 is adjusted along path 36.

The materials of Kerr Cell 22 and Kerr Cell 24 are

different and may be chosen so that the difference in optical rotation for the two together rotates the anticipated range of fluorescent wavelengths by about the same angle on traversal whereas the rotation of the reflected excitation light is rotated by a substantially different amount.

Alternatively it may be chosen so that the rotation angle is wavelength independent. In these latter cases separation between fluorescent wavelengths (and reflection) is achieved by means of lens 46 and prism 48, and separate channels of acquisition are obtained from separate photodetectors 44 and 50.

Figure 2 is a schematic view of the optical configuration of an endoscope head 52 according to a further preferred embodiment of the present invention. The head 52 includes first lens 54 for collimating blue laser excitatory beam 56. Collimated beam 58 passes through prism 60, and is then focussed to a Gaussian waist 62 (in use, within a sample) by second lens 64.

Return light will retrace the incoming light back to prism 60, but will be refracted through a different angle owing to its different wavelength; hence prism 60 will act as a beam splitter, and the return light 64 will emerge from first lens 54 separated from incoming beam 56.

The head 52 of figure 2 is very simple, but the angular deflection at the prism and hence non-linear optic axis may - in some applications - be disadvantageous, as it imposes a shape for the head which may be inconvenient to use or make it difficult or impossible for the head to pass through a narrow tube.

An optical configuration of an endoscope head according to a further preferred embodiment of the present invention is

shown in schematic form in figure 3 at 66. The head 66 includes a prism combination 68 (to give a straight through optic axis and a straight cylindrical head for the endo- or endomicroscope design) as well as first and second lenses 70 and 72. Again, return light 74 emerges from first lens 70 separated from incoming excitatory beam 76.

Prism combination 68 utilises the same principle as an achromatic doublet except that the angles are reversed to give minimum deviation but maximum dispersion.

An optical configuration according to a further preferred embodiment of the present invention is shown in schematic form in figure 4 at 78. The head 78 includes a direct vision spectroscope three prism combination 80 and is comparable (though in reverse) to a Hastings achromatic triplet, to reduce or eliminate astigmatism resulting from the arrangement of figure 3. Prism combination 80 includes a 60° SF11 Flintglass central prism 82 cemented between two 45° BK7 prisms 84 and 86. This arrangement gives almost 0° deviation for the blue laser line and considerable overall dispersion, between incoming excitatory beam 88 and return beam 90.

Figure 5 is a ray trace for the prism combination 80 or figure 4, showing central 60° SF11 Flintglass prism 82 between the pair of 45° BK7 prisms 84 and 86. Incoming beam 92 will be dispersed into an undeviated component 94, with the red deviated as shown at 96 and blue at 98. The total dispersion of this particular combination 80 is greater than would be required for a miniature endomicroscope head and prisms of much smaller angles (and shorter overall dimensions) may be suitable and, in some applications, preferable.

Figure 6 is a schematic representation of an optical

configuration 100 for an endoscope head according to a further preferred embodiment of the present invention. The configuration 100 includes a combination of plano-concave and plano-convex lenses 102 and 104, optically coupled together to give a system in which the divergence of the return beam 106 relative to the incoming excitatory beam 108 can be almost infinitely varied, but altering the position of plano-convex lens 104 within the concavity of plano-concave lens 102. This configuration 100 also includes collimating lens 110, focussing lens 112 and prism pair 114 located between plano-convex lens 104 and focussing lens 112.

The embodiments of figures 2, 3, 4 and 6 have the advantage of simplicity but suffer from the drawback that the return light fluorescence, even from a single pure fluorophore, consists of a broad range of wavelengths, which does not focus to a spot but spreads into a spectral line. This makes collection by the return fibre more difficult (a line of fibre cores or a fibre bundle is required or special fibre design with elongated collection aperture means) and also reduces the isolation of the focal plane to an equivalent value for a slit scanning confocal system.

There is a way of getting around this using a prism based system in the head. The common optical glasses including the Flint glass Crown glass pair SF11 and BK7 referred to earlier are made from glass types which fall on Abbe's 'normal' glass line. On this line the partial dispersions of the glasses match in a way which allows doublet lenses to be constructed which are achromatic for the visible region 400-700 nm (a likely requirement of lenses for human use). Any pair of glasses from this line can be combined in a concave convex doublet (suitably matched) to produce an achromatic lens combination.

There are glass types available which do not follow the Abbe's 'normal' glass line, that is their partial dispersions do not match and they are said to have deviating partial dispersions (see Schott Tables). These glasses are formulated to correct the slight secondary spectrum (green-orange) which remains in achromatic doublets because the partial dispersions even of the normal line glasses never exactly match for all wavelengths. In a lens design the addition of an appropriately figured third lens of such a glass type allows the spectral curves to match at three levels and thus greatly reduces the secondary spectrum. Such lenses are known as 'apochromatic'. Apochromatic lenses have many more individual lens elements in them (up to 20 in some cases) to correct for other aberrations.

After an appraisal of the spectral deviation curves, one can choose such a glass to replace the BK7 crown prism, and combine this replacement with an SF 11 or SF 59 prism to produce a combination which is reasonably achromatic and non-deviating for the 515-650 nm range but which has substantial dispersion for the blue.

Such a prism pair will produce a good separation between the blue 488nm excitation line and the fluorescence. The fluorescence spectrum is effectively bunched up although the graph is not entirely level but folds back (the angular deviation will actually only be exactly the same for matching pairs of wavelengths). However, this is a considerable improvement. A third glass type taken from another line on the Abbe deviation glass curve will produce even further flattening, and sets of three wavelengths will have exactly matchings angular deviations.

A fourth prism of suitably chosen glass could be added to further correct the spectrum to four wavelengths as shown

in figure 7 (which comprises a direct vision prism pair 116 comprising four prisms 118a,b,c,d).

Such a combination of prisms could be made from standard Schott catalogue optical glasses. Fortunately it is much easier to find standard glass types which have appropriate RI deviation in the blue than the red, but the number of prisms required could be reduced and the design made more compact by the choice of special optical materials. Such materials could include fluorite (CaF_2) or magnesium fluoride in combination with a second optical material that exhibits strong anomalous dispersion.

It is also possible to design an optical material for the second prism with a more strongly kinked anomalous deviation curve, which would minimise the number of prisms (possibly to just two) and their angle and hence the optical thickness. The specifications would be that the material is glassy or isotropic (cubic crystal structure), that it has an intrinsic absorbance or a dopant which absorbs in the indigo/violet part of the spectrum, shorter than 488nm, so that the positive asymptotic limb of the anomalous dispersion curve lifts the deflection angle from the 488nm but has the dispersion uniform and of much lower gradient for the 515-650nm region.

The optical medium or dopant must not fluoresce or have too high an absorption at the excitation wavelength and should be free of absorption lines in the 515-650 nm fluorescence region. Suitable materials include certain organic dyes dissolved in transparent polymer or might potentially be formulated from a rare earth doped fluorozirconate ZBLAN glass.

This principle of successive corrections by a train of optical elements and the use of 'kinks' in the active parameter graphs (the relevant equivalent to anomalous

dispersion in other optical properties) can be applied to a number of other novel beam splitter methods and apparatuses according to the present invention.

For example, figure 8 is a schematic view of an endoscope head 120 with a beam splitter 122 based on optical rotary dispersion in a chiral medium. This beam splitter depends on the optical rotatory dispersion of a medium containing chiral molecules or chirally oriented bonds, such as glucose or $NaClO_3$.

The explanation which follows is couched for an embodiment in which a liquid is used as the optically active medium although in practice this may require an excessive path length and a chiral crystal (such as quartz), cut with faces orthogonal to the C axis, may be preferred, as optically active (chiral) crystalline materials have a far greater rotating power than most liquids; quartz, for example, has a rotating power of 21.7° per mm whereas dextrose syrup has a rotating power of 1° per mm.

The operation of this method requires the light to be polarised in a fixed vector state as from a laser diode and hence polarisation maintaining fibre is needed if the design is adapted to a two fibre system.

The polarised light 124 emitted from a laser diode (not shown) is collimated by lens 126 and passes through a prism pair in the form of SWF 128. The SWF 128 is oriented so that the eigen-vector of the light is parallel to the prism's fast (or slow) axis. This differs from Nomarski microscopy in which the polarisation vector is oriented at 45° to the fast and slow axes of prism and the beam is split 50:50. Thus, in this embodiment the light is not split into separate orthogonal polarisation beams on its first traversal of the SWF 128.

The beam next passes into a tube or column 130 of dextrose syrup (d glucose), which rotates the plane of the polarisation vector in a right handed spiral by a certain amount, preferably > π radians. The light beam exits the flat face 132 of the far side of the tube 130 and passes to an objective lens 134, which focuses the beam to a Gaussian waist 136 within the specimen (not shown).

Fluorescence generated at the Gaussian waist 136 is Stokes shifted but is in general predominantly of the same polarisation vector state as the polarisation vector of the excitation beam (as long as the relaxation time of the excited state of the fluorophore is not too long).

Some of this light and some of the excitation wavelength reflected from the region passes back through the objective lens 134 to the dextrose column 130. Reflection from most materials does not alter the polarisation vector.

In traversing the column 130 in the reverse direction the polarisation vector is again rotated in a right handed spiral, rotating backwards by exactly the same angle by which it was rotated forwards on its first pass. The fluorescent light is also rotated in a right handed spiral direction but, because of optical rotatory dispersion (that is, as the interaction strength between the spiral mechanical oscillators is wavelength dependent), it is rotated through a different angle to the reflected beam.

For the most efficient operation of the beam splitter 122, the difference between the optical rotatory dispersion angles of the reflected light and the fluorescence should be $\pi/2$.

After traversing the chiral medium in column 130, the light then passes back to the prism pair 128. In this

embodiment, prism 128a is made of a birefringent material such as calcite, cut and polished at a suitably oriented crystal angle. The reflected return light acts as the 'ordinary' ray and is refracted by the prism 128a along exactly its initial path to its point of origin. The fluorescent return light - having its polarisation vector at $\pi/2$ relative to the reflected ray - acts as the 'extraordinary' ray and is deflected by a different angle when it passes the prism 128a. This prism 128a also introduces a slight chromatic dispersion as well because the fluorescence consists of a range of wavelengths. This dispersion of the fluorescence is compensated for by the matching dispersion of the second prism 128b (the next element traversed by the returning light). The light is then focussed by the lens 126 and the confocal return enters the core of the return fibre 138 and is transmitted along the fibre to a photodetector (not shown).

Note: where referred to below, the SWF is employed in a similar fashion in the following apparatuses and the description here will cover these systems as well.

This principle can operate for Argon Krypton lasers with two or more laser excitation wavelengths simultaneously traversing the dextrose column. Each wavelength will be rotated on its first traversal and after reflection, its rotation exactly reverse spiralled on return to the original source. The fluorescence from each excitation wavelength will be rotated by a different angle on return and therefore a portion of the fluorescence from each excitation wavelength be deflected at the extraordinary angle at the birefringent prism so as to enter the second fibre.

As another improved embodiment it is possible to choose a second optically active medium in the opposite enantiomorphic form which had an optical rotating

dispersion curve which matched dextrose for the green, yellow and orange wavelengths but which kinks markedly for the blue, and to combine this to produce an 'achromatisation' of the fluorescence but a separation of the excitation wavelength. For example, laevulose (the laevo enantiomorphic form of glucose) produces a left handed rotation of the plane of the polarisation vector of light passing through it. This opposes the rotation of the dextrose and, where the optical rotating dispersion curve of laevulose had a different gradient compared to dextrose (analogous to the refraction dispersion curves of the flint glass prism of the previous design), it is suitable for this purpose. Laevulose does not have the required kink in the graph for blue, but other substances do.

Quartz is a uniaxial crystal type and this may result in problems for certain scanning embodiments. For example if the scanning is carried out by means of a rastered movement of the blue laser chip or of the fibre tip then the beam will, for much of the time, propagate through the quartz crystal plate at a slight angle to the C axis. This will introduce birefringence into the optical path and consequent eigenvector separation which will add extra complexity and reduce optical efficiency. There are optical materials (such as sodium chlorate crystals) which are optically active, but not birefringent which would avoid this difficulty. The rotary power of this material is 3.1° per mm (for the sodium yellow lines) which is rather low for some applications. Materials with much higher optical rotatory power are detailed below.

In another preferred embodiment of the present invention, the Faraday effect is used to provide the desired beamsplitting (that is, the rotation of the E vector of linearly polarised light as it passes through a material which simultaneously has magnetic lines of force in the

same direction as the propagation direction of the light). The optical rotator of a beam splitter according to this embodiment is shown at 142 in figure 9. The optical rotator 142 includes a cylindrical piece of glass 144 (chosen to have a high Verdet constant) with flat polished AR coated ends 144a surrounded by a tubular cylindrical magnet 146 with north face N and south face S. The beam splitter (like those described below) is otherwise like beam splitter 122 of figure 8 with a birefringent prism acting as the beam separation element (but with the optical rotator replacing the column 130). As the beams of light traverses the optical rotator, the magnetic field of magnet 146 progressively rotates the E vector. Faraday rotation differs from chiral optical activity in that the reflected light undergoes further rotation of the E vector in the same direction when retraversing the glass 144. This is a non-reciprocal effect unlike chiral rotation in which the spiral retraces its original path on reflection.

This difference is important because it means that the beam splitter can be tuned to obtain maximum rotational efficiency of the reflected beam, that is 45° E vector rotation from each traversal, thus minimizing the required thickness of the glass 144. Also, as the Verdet constant is wavelength dependent the system can be switched from fluorescence to reflection.

The variation in magnetic field strength required to carry out these functions can be achieved by varying the electrical current in a wire coil wound around the glass cylinder 144 or by sliding the magnetic cylinder 146 in an axial direction so that a greater or lesser magnetic field interaction length with the active glass medium 144 can be effected. The Verdet constant is generally greater for short wavelengths and as the dependence curve shapes vary for different materials it is possible using suitable combinations to arrange a maximum rotation for the blue

excitation wavelength and a compressed range of rotation for the fluorescence. This will result in the most efficient use of light.

In another preferred embodiment of the present invention, the beam splitter of the endoscope includes phase plates (or retardation elements): optical elements of a material with a physical structure that is anisotropic at a molecular or crystalline level. In classical optical terms, the spring stiffness of the mechanical oscillators in the two orthogonal polarisation states is different because of the differing bond types or degree of strain within bonds in the two directions. This means that the velocity of propagation of electromagnetic vibration in the visible region differs for the two orthogonal polarisation vector directions, the material is said to be birefringent, that is, having two Indices of Refraction. The two directions of the crystal plate are called the fast axis and the slow axis. (The two sets of electromagnetic propagation direction are sometimes called the ordinary and extraordinary) - o and e rays. (Note the E vector used previously stands for electric field vector).

Birefringent prisms are commonly made from uniaxial crystals (e.g. calcite) and their use to separate light beams of orthogonal polarisation state has been described above.

A phase plate is effectively a 'parallel sided prism' of a birefringent material. If light impinges at right angles to the waveplate surface there is no deviation between the e and o ray, but waves with the E vector parallel to the slow axis are retarded relative to waves with the E vector parallel to the fast axis. A plane polarised wave entering the plate at an intermediate angle between the slow and the fast axes is resolved vectorially

into two orthogonal polarisation states which propagate at different velocities (and with different wavelengths, their frequency being constant). The two waves leave the waveplate with relative phase shift. The polarisation state of the light when it leaves the wave plate is determined by the phase angle.

Anisotropy and phase shifting can also be induced and tuned in isotropic materials by straining the interatomic bonds either with a mechanically applied force, (stress induced birefringence) or by the application of a voltage between plates which produces and electrical field (the optical Kerr effect) and these principles could also be applied to a tuneable beam splitter for confocal use.

In another embodiment of the present invention, liquid crystal systems are employed to rotate light within the endoscope head optically. Liquid crystals can be optically active, birefringent, or both, so their principles of operation is covered in the two previous embodiments. The rotatory power of cholesteric liquid crystals is very large of the order of 40,000° per mm compared with ~1° per mm for corn syrup and 21.7° per mm for quartz. The major advantage of using liquid crystal systems, therefore, is the compactness possible, and their being electrical controllable and tuneable. Liquid crystal display screens use nematic liquid crystals and these are commercially available made up as electrically controllable variable phase retarders. A supertwisted nematic liquid crystal 'valve' could be used as an electrically controllable tuning device for reflection confocal microscopy. It would also have enough rotation in the 'power off' mode to give colour separation for fluorescence imaging.

In another preferred embodiment of the present invention, the intrinsic polarisation properties of the reflecting

object (or of the intermediate optical medium) is used to obtain optical rotation between excitatory and return light, as many biological materials exhibit birefringent properties and/or produce optical rotation.

Figure 10 is a schematic view of the head of a confocal endoscope 150 according to a further preferred embodiment of the present invention, shown with a specimen 28. This embodiment is, in many respects, similar to that depicted in Figure 1 and accordingly like reference numerals have been used to refer to like features. In the embodiment in Figure 1, the miniature laser diode 12, astigmatism corrector 16 and tip of optic fibre 40 are mounted on scanning mechanism 14. This is also so in confocal endoscope 150, but beam splitter 152 is also mounted by means of mounting arm 154 on scanning mechanism 14. Thus, in use, the beam splitter 152 is scanned (typically vibrated) with the laser 12 and tip of the optic fibre 40.

This configuration maintains the beam splitter 152 in a constant position in the optical path as the optical path is moved by scanning mechanism 14 and allows the head of confocal endoscope 150 to be particularly compact.

Figure 11 is a schematic view of an alternative preferred beam splitter according to the present invention. In this embodiment, a miniature laser diode 160 is provided, together with mirror 162, on a single silicon substrate 164. The incident beam 166 from the laser diode 160 is reflected towards focusing lens 168. Lens 168 then focuses the beam to a Gaussian waist within a specimen (not shown).

Return light from the specimen retraces the beam path but, as the return light comprises a broader distribution of wavelengths, only a portion of the return light will be incident on mirror 162. Some of the return light will

pass beside mirror 162, to be detected by a photodiode 170 located adjacent to mirror 162.

Thus, in this embodiment the beam splitter is provided by the combination of adjacent photodiode 170 and mirror 162.

Further modifications within the spirit and scope of the invention may readily be effected by person skilled in the art. It is to be understood, therefore, that this invention is not limited to the particular embodiments described by way of example hereinabove.

WHAT IS CLAIMED IS:

1. A confocal endoscope or microscope including:

a light source of coherent light for illuminating a sample;

a beam splitter; and

light receiving means, wherein an incident beam of light from said light source is directed onto said beam splitter and hence onto said sample, and light returning from said sample and incident on said beam splitter is deviated or displaced by said beam splitter by a small angle or distance relative to said incident beam, and received by said light receiving means located to receive said returning light and near said light source.

2. A confocal endoscope or microscope as claimed in claim 1, including an optical head and said light source is located in or on said head.

3. A confocal endoscope or microscope as claimed in claim 2, including heating means for maintaining said head at a temperature substantially equal to that of said sample.

4. A confocal endoscope or microscope as claimed in claim 1, wherein said light source and said light receiving means are on a single mounting means.

5. A confocal endoscope or microscope as claimed in claim 4, wherein said beam splitter is mounted on said mounting means.

6. A confocal endoscope or microscope as claimed in claim 4, wherein said mounting means is moveable for scanning said light source.

7. A confocal endoscope or microscope as claimed in claim 4, wherein said mounting means includes a reed.

8. A confocal endoscope or microscope as claimed in claim 4, wherein mounting means is an electromagnetically vibrated reed.

9. A confocal endoscope or microscope as claimed in claim 1, wherein said light source and said light receiving means are adjacent or touching.

10. A confocal endoscope or microscope as claimed in claim 1, wherein said light source is an optical fibre tip.

11. A confocal endoscope or microscope as claimed in claim 1, wherein said beam splitter includes a plurality of prisms and/or lenses.

12. A confocal endoscope or microscope as claimed in claim 11, wherein said plurality of prisms and/or lenses provide minimal net deviation or translation, so that said coherent light or light reflected from said sample emerges from said plurality of prisms and/or lenses substantially parallel to and optically coaxial with its path immediately before impinging said plurality of prisms and/or lenses.

13. A confocal endoscope or microscope as claimed in claim 11, wherein said plurality of prisms and/or lenses is arranged to focus confocal return stokes fluorescence to form a line, said line forming a spectrum in which shorter wavelength fluorescence is located towards a first end of said line closer to said light source, while longer wavelength fluorescence is located towards a second end further from said light source.

14. A confocal endoscope or microscope as claimed in claim 1, including means to allow light on either side of

a spectral line in said returning light to be included with light from said spectral line when said returning light impinges on said light receiving means.

15. A confocal endoscope or microscope as claimed in claim 14, wherein said means is controlled by a mechanism which occludes light which is more distant in wavelength than a desired amount from said spectral line, to allow control of depth of field isolation.

16. A confocal endoscope or microscope as claimed in claim 1, including optical elements to divert chosen wavelength portions of said spectral line, and optionally light close in wavelength to said spectral line, to one or more photodetectors to give different spectral channels for imaging.

17. A confocal endoscope or microscope as claimed in claim 1, including at least one optical waveguide channel to convey said returning light to said photodetectors.

18. A confocal endoscope or microscope as claimed in claim 1, including a laser and an optical waveguide to convey light from said laser to said light source.

19. A confocal endoscope or microscope as claimed in claim 1, including a first optic waveguide to convey light to said specimen and at least one second optic waveguide channel to convey said returning light to said photodetectors, and said beam splitter is disposed in said head between said first and second optic waveguides.

20. A confocal endoscope or microscope as claimed in claim 1, including a return fibre and wherein said beam splitter is located between a light exit area of said return fibre and said photodetectors, to provide spectral separation after said returning light exits said fibre.

21. A confocal endoscope or microscope as claimed in claim 1, including an aperture slit moveable in front of said photodetectors simultaneously with said scanning to compensate for changes in beam splitter deviation.

22. A confocal endoscope or microscope as claimed in claim 11, wherein said plurality of prisms and/or lenses include at least one apochromatic lens.

23. A confocal endoscope or microscope as claimed in claim 11, wherein said prisms and/or lenses include an SF 11 or SF 59 prism.

24. A method for performing confocal endoscopy or microscopy including:

illuminating a sample by means of an incident or excitatory beam of coherent light; and

deviating or displacing light returning from said sample by a small angle or distance relative to said incident beam.

25. A method as claimed in claim 24, including receiving or detecting said returning light at a point close to a source of said incident or excitatory beam.

26. A method as claimed in claim 24, wherein said deviating or displacing of said light returning from said sample is effected by means of a beam splitter.

27. A confocal endoscope or microscope including:

a light source of coherent light for illuminating a sample;

a beam splitter; and

light receiving means, wherein an incident beam of light from said light source is directed onto said beam splitter and hence onto said sample, and light returning

from said sample and incident on said beam splitter is deviated by said beam splitter by a small angle relative to said incident beam, and received by said light receiving means located to receive said returning light and near said light source, and said beam splitter includes polarisation rotating means and deviation means to separate light of different polarisations, and operates by optically rotating said coherent light and said returning light.

28. A confocal endoscope or microscope as claimed in claim 26, wherein said polarisation rotating means is based on optical rotary dispersion and includes a chiral medium to optically rotate said coherent light and said returning light.

29. A confocal endoscope or microscope as claimed in claim 27, wherein said polarisation rotation means includes a Faraday effect material, said material having simultaneously magnetic lines of force in the same direction as the propagation direction of said light, whereby the E vector of said coherent light is rotated as it passes through said material .

30. A confocal endoscope or microscope as claimed in claim 27, wherein said polarisation rotation means includes phase plates or retardation elements, of a material whose structure is anisotropic at a molecular or crystalline level.

31. A confocal endoscope or microscope as claimed in claim 27, wherein said polarisation rotation means includes liquid crystals.

32. A confocal endoscope or microscope as claimed in claim 31, wherein said liquid crystals are optically active and/or birefringent.

33. A confocal endoscope or microscope as claimed in claim 31, wherein said liquid crystals are cholesteric liquid crystals.

34. A confocal endoscope or microscope as claimed in claim 25, wherein said optical rotation is provided by intrinsic polarisation properties of the sample or of any intermediate optical medium.

35. A method for maintaining registration in a confocal endoscope or microscope including a light source and a light receiving means, including:

splitting light returned from a sample with a small angle deviation beam splitter;

employing said light source and said light receiving means located on a single moveable mounting means;

moving said mounting means to scan said light source and thereby said sample.

36. A method as claimed in claim 35, wherein said beam splitter includes a plurality of prisms and/or lenses.

37. A method as claimed in claim 36, wherein said plurality of prisms and/or lenses provide minimal net deviation.

38. A method as claimed in claim 36, including moving said beam splitter with said light source and said light receiving means.

39. A method as claimed in claim 35, wherein said moving of said mounting means comprises vibrating said mounting means.

40. A method as claimed in claim 35, wherein said mounting means is a reed.

41. A method as claimed in claim 35, wherein said mounting means is an electromagnetically vibrated reed.

42. A confocal endoscope or microscope as claimed in claim 1, wherein said light source comprises a mirror located in the path of the returning light for directing light towards said sample, wherein said mirror has a smaller solid angle than said returning light to only partially occlude reception of said returning light by said light receiving means.

43. A confocal endoscope or microscope as claimed in claim 42, wherein said mirror and said light source are provided on a single piece of silicon and said mirror comprises an etched mirror surface of the silicon.

44. A method for performing confocal endoscopy or microscopy including:

illuminating a sample by means of an incident or excitatory beam of coherent light and thereby inducing a broader beam of returning light; and

detecting a portion of said returning light adjacent to or near said incident beam.

45. A method as claimed in claim 44, including directing said incident light towards said sample by means of a mirror located in the path of said returning light, wherein said mirror has a smaller solid angle than said returning light to only partially occlude reception of said returning light.

46. A method as claimed in claim 45, wherein said mirror and the source of said incident light are provided on a single piece of silicon and said mirror comprises an etched mirror surface of the silicon.

ABSTRACT

The present invention provides a confocal endoscope, microscope or endomicroscope including a light source of coherent light for illuminating a sample, a beam splitter and light receiving means, wherein an incident beam of light from the light source is directed onto the beam splitter and hence onto the sample, and light returning from the sample and incident on the beam splitter is deviated or displaced by the beam splitter by a small angle or distance relative to the incident beam, and received by the light receiving means located to receive the returning light and near the light source. The invention also a method for performing confocal endoscopy or microscopy including illuminating a sample by means of an incident or excitatory beam of coherent light, and deviating or displacing light returning from the sample by a small angle or distance relative to the incident beam.

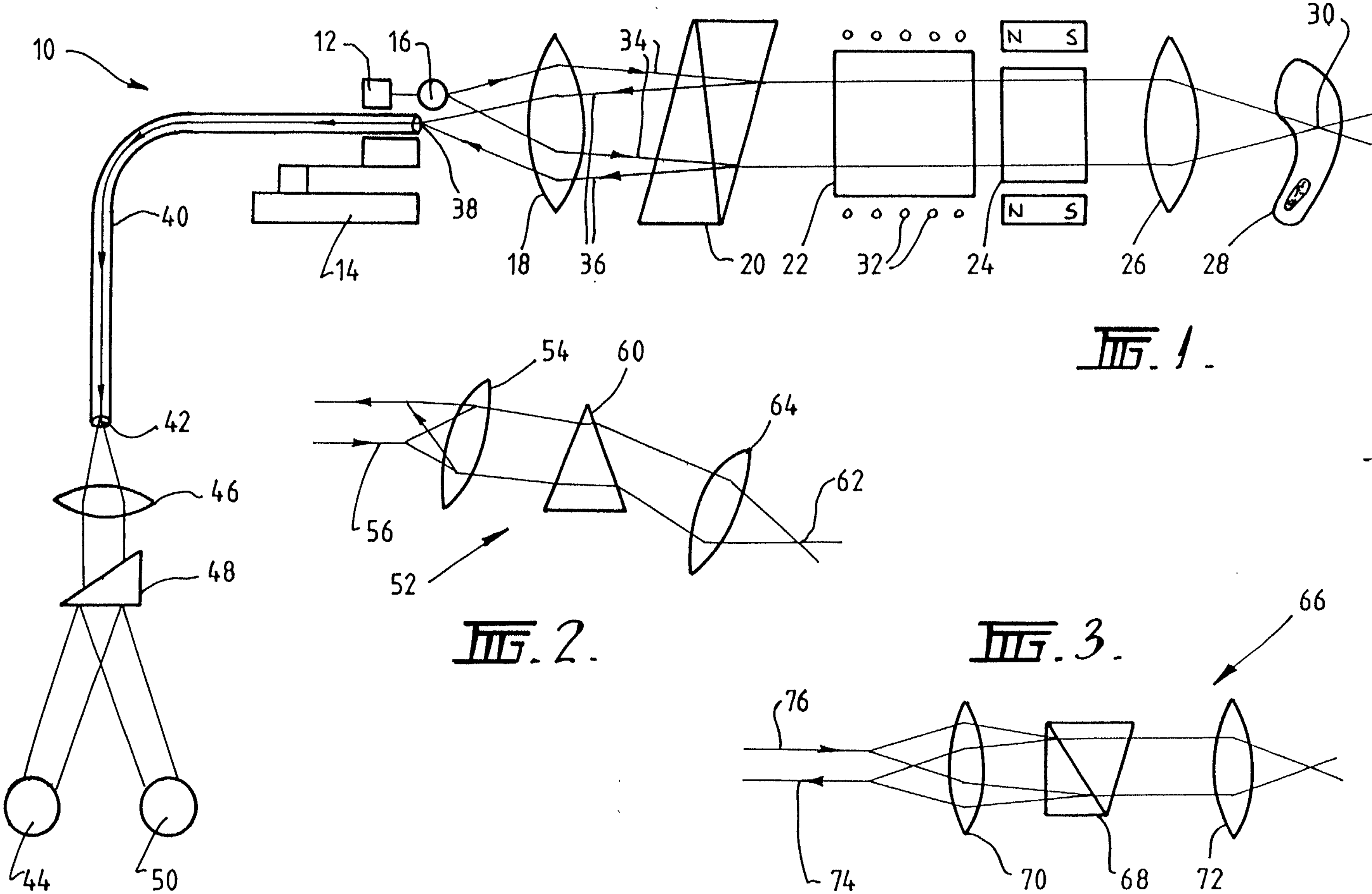

FIG. 1.

FIG. 2.

FIG. 3.

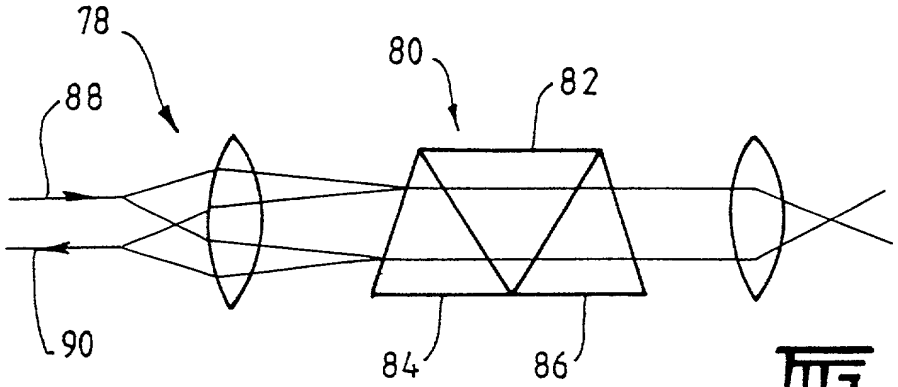

FIG. 4.

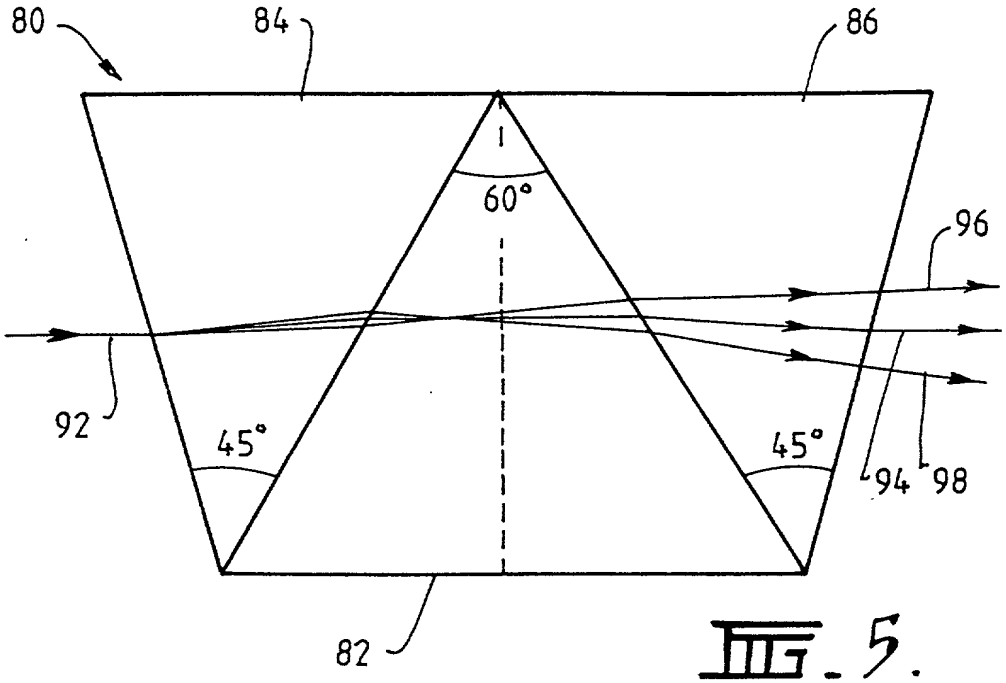

FIG. 5.

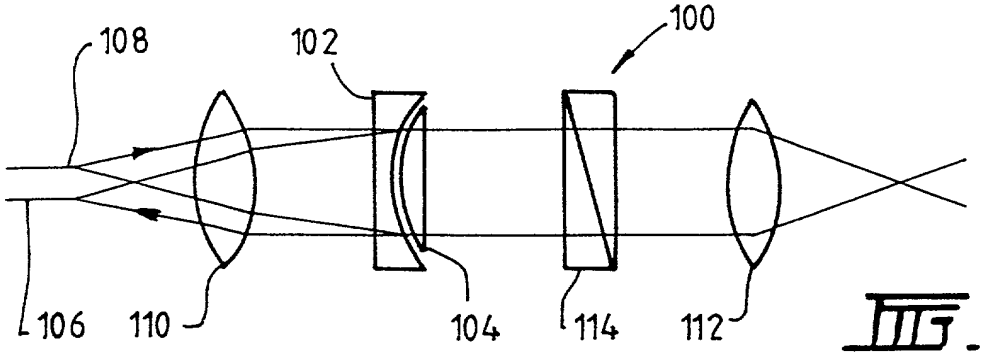

FIG. 6.

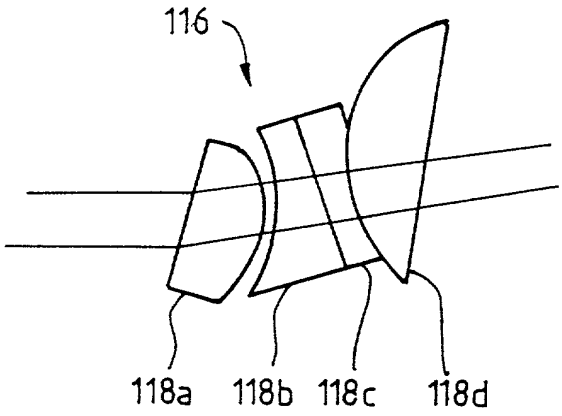

FIG. 7.

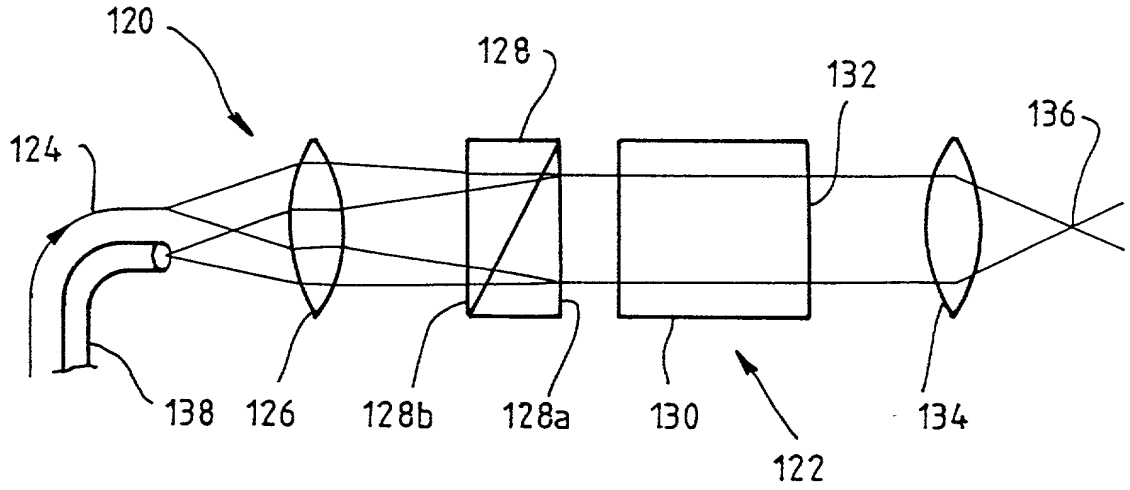

FIG. 8.

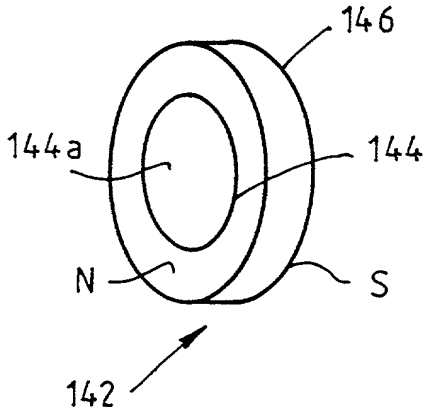

FIG. 9.

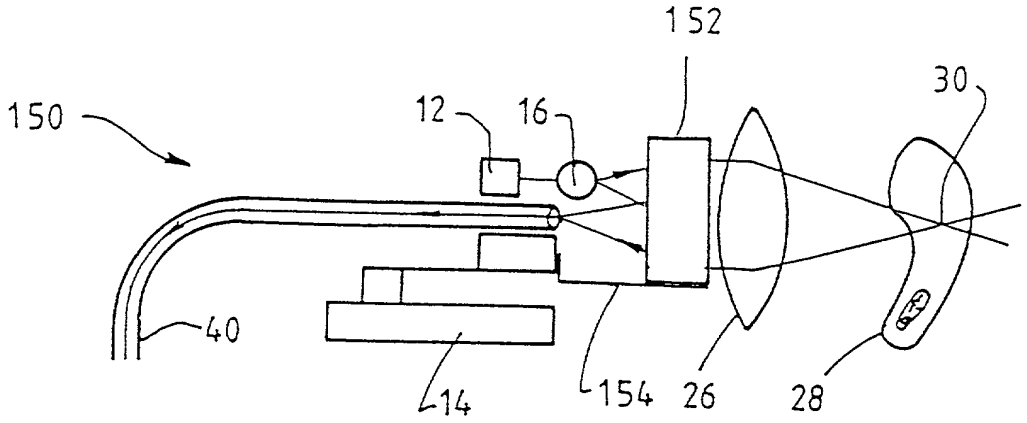

FIG. 10.

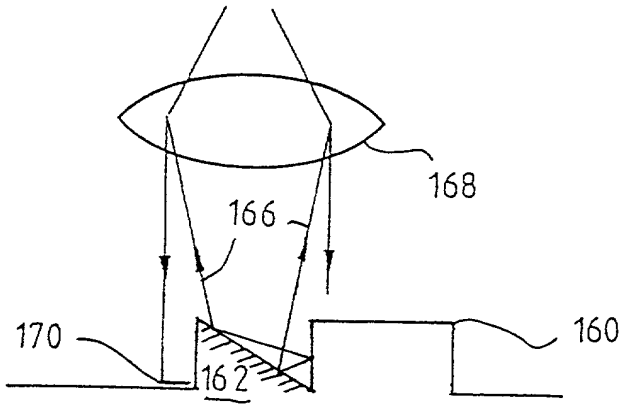

FIG. 11.

DECLARATION FOR USA PATENT APPLICATION

(including Design and National Stage PCT) Attorney's Docket ID: _____

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below adjacent to my name. I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought

on the invention entitled: COMPACT CONFOCAL ENDOMICROSCOPE AND ENDOMICROSCOPE METHOD AND APPARATUS

the specification of which:

X is attached hereto.

(or)

___ was filed on _____, was amended on _____ (if applicable), and was filed

as U.S. Application No. or PCT International Application No. _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment specifically referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below, where priority is not claimed, any foreign application for patent or inventor's certificate, or any PCT International application, having a filing date before that of the application on which priority is claimed. (___ ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET)

Prior Foreign Application No.	Country	Day/Month/Year Filed	Priority *NOT* Claimed
PP5482	AUSTRALIA	27/8/1998	___
			___

I hereby claim the benefit under 35 U.S.C. 120 of any U.S. application(s), or 365(c) of any PCT application designating the U.S., listed below; and insofar as the subject matter of each claims of this application is not disclosed in the prior U.S. or PCT application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT filing date of this application. (___ ADDITIONAL APPLICATIONS IDENTIFIED ON ATTACHED SHEET.)

U.S. or PCT Parent Application No.	Parent Filing Date (Day/Month/Year)	Parent Patent No. (if applicable)

As a named inventor, I hereby appoint the registered practitioners of **LARSON & TAYLOR** associated with **Customer Number 000881** to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith. Direct all correspondence to that Customer Number.

000881

Direct all telephone calls to _____, at TEL (703) 739-4900 (Fax: 703-739-9577) E-Mail:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1000 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SOLE OR FIRST INVENTOR	Citizenship: AUSTRALIAN
Given Name (first and middle [if any]): MARTIN RUSSELL	Family Name or Surname: HARRIS
Full Post Office Address: 163 PEEL STREET, WINDSOR VICTORIA 3181, AUSTRALIA	
Residence - City, State/Country (if different from P.O. address)	
SIGN AND DATE HERE: Inventor's Signature: Martin Harris	**Date:** 28th July 1999

SECOND JOINT INVENTOR [if any]	Citizenship
Given Name (first and middle [if any])	Family Name or Surname
Full Post Office Address	
Residence - City, State/Country (if different from P.O. address)	
SIGN AND DATE HERE: Inventor's Signature:	**Date:**

THIRD JOINT INVENTOR [if any]	Citizenship
Given Name (first and middle [if any])	Family Name or Surname
Full Post Office Address	
Residence - City, State/Country (if different from P.O. address)	
SIGN AND DATE HERE: Inventor's Signature:	**Date:**

FOURTH JOINT INVENTOR [if any]	Citizenship
Given Name (first and middle [if any])	Family Name or Surname
Full Post Office Address	
Residence - City, State/Country (if different from P.O. address)	
SIGN AND DATE HERE: Inventor's Signature:	**Date:**